

The Avian Influenza H5N1 Threat

Current facts and future concerns about Highly Pathogenic Avian Influenza H5N1.

A highly pathogenic strain of avian influenza called H5N1 has caused mortality in over 40 species of wild birds including herons, storks and falcons in Asia. Millions of domestic poultry have either died or been culled in Asia because of outbreaks of highly pathogenic avian influenza (HPAI). Concern about wild birds infected with H5N1 increased when migratory waterfowl, including bar-headed geese, brown-headed gulls and great black-headed gulls, began dying at Qinghai Lake Nature Reserve in western China and were discovered in May 2005. Over 6,000 birds have died so far. Studies showed that these birds were infected with HPAI H5N1 and that the Qinghai H5N1 strain appears to be a new recombinant virus, combining genetic material from at least two other HPAI H5N1 strains. It is unknown whether waterfowl and shorebird species infected with the current strains of H5N1 will become reservoirs and

whether they will become carriers of the virus during migration.

Typically, wild birds, such as migratory waterfowl, rarely show signs of the disease. However, some strains, such as H5N1, can cause serious illness and mortality in commercial poultry flocks. Not only is this strain of avian influenza in Asia highly pathogenic to domestic poultry, it can directly infect people and is capable of causing mortality in wild birds. There is growing concern that H5N1 may evolve into a strain that could spread over a larger geographical area by infecting migratory waterfowl and/or transmit efficiently from human to human, leading to a global pandemic.

Influenza can be divided into three groups (Types A, B, and C). Type A virus causes infection in birds (referred to as avian influenza or "bird flu"), humans, and some mammals, such as pigs; Type B is found exclusively in people; and Type C occurs



Bar-headed goose. Many bar-headed geese died in an H5N1 outbreak in Qinghai Lake Nature Reserve in China.

in humans and pigs. Two proteins on the surface of Type A, hemagglutinin (HA) and neuraminidase (NA), are essential for infectivity. Protective immunity is developed when antibody is developed against these proteins, which are the basis of influenza vaccines. There are 16 different types of HA and 9 different types of NA known. Human infections have been caused mainly by influenza viruses containing the H1, H2 and H3, and N1 and N2 proteins. In 2004–2005, H1N1 and H3N2 were the main influenza A strains circulating in humans.

Wild birds, especially shorebirds and waterfowl, are the natural reservoir of influenza A viruses. The birds and the virus have become well-adapted to each other over time; infection does not usually cause overt disease in wild birds. Unlike in humans, where only a limited variety of influenza subtypes are present, viruses of all HA and NA subtypes are found in aquatic birds. The viruses replicate mainly in the intestinal tract of aquatic birds and are transmitted in the feces. Thus, unlike human-to-human transmission, which is mainly via aerosol, transmission in aquatic birds is by the fecal-oral route. Avian influenza strains from wild birds usually cause mild, inapparent disease in domestic poultry and are designated low path avian influenza viruses (LPAI). Commercial poultry farms raise

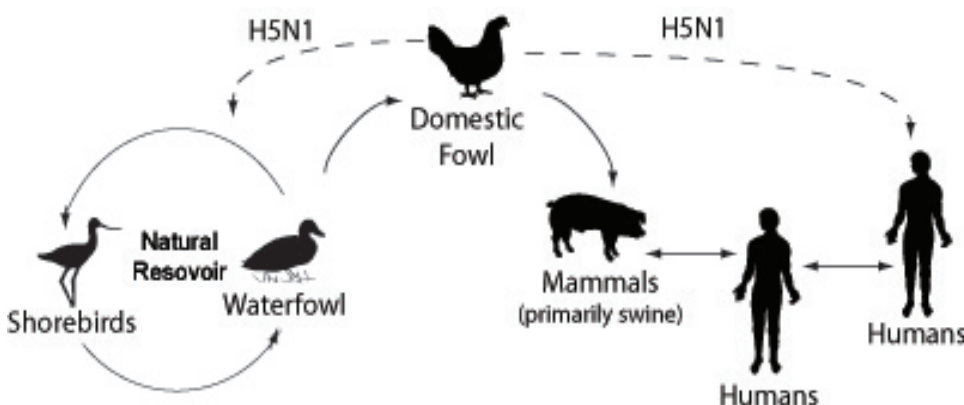


Figure 1. Possible transmission pathways for avian influenza.

thousands of birds in close proximity, which allows avian influenza viruses to replicate efficiently. As the influenza viruses change during replications in the domestic poultry, highly pathogenic avian influenza (HPAI) strains can arise, resulting in severe disease and high mortality.

The genetic material of the influenza A virus is constantly changing and small-scale mutations (genetic drift) in the HA and NA proteins that alter antibody recognition lead to viruses that can evade the immune response. Although slightly different, viruses with such genetic drifts may still belong to the same subtype. For example, these two subtypes, A/chicken/Shantou/423/2003 (H5N1) and A/bar-headed goose/Qinghai/5/2005 (H5N1) are still considered H5N1, but differ in a number of ways. In this longer, more specific nomenclature for influenza A strains, the “A” refers to the influenza type; this is followed by the animal species from which the virus is isolated; the geographical location; a laboratory strain designation; the year of isolation; and then the abbreviated HA and NA subtype. Previous exposure to and/or vaccination with the same subtypes that have genetic drift differences, confers only partial protection against the virus. For example, in the U.S. during 2004–2005, the flu vaccine contained the H3N2 strain A/human/Fujian/411/2002 (H3N2), but individuals may want to be vaccinated with the 2005–2006 vaccine, containing A/human/California/7/2004 (H3N2), as the virus

that is in circulation has undergone genetic drifts over time. Similarly, in birds, the H5N1 strain originally identified in Hong Kong in 1997 was highly pathogenic to chickens, but was inefficient in infecting ducks. Whereas, the H5N1 strains isolated since 2002 are well-adapted to ducks; in fact, researchers have found that a number of different strains of H5N1 are now simultaneously circulating in Asia.

Large-scale changes (genetic shifts) occur when the influenza A virus recombines with genetic material from two or more strains, leading to the emergence of influenza virus with a novel hemagglutinin subtype. The abrupt shift of hemagglutinin into a different subtype has led to pandemics, because there is no protective immunity in the population and the virus spreads rapidly from person to person across the globe. In the twentieth century, the world experienced three pandemics, H1N1 (1918–1919), H2N2 (1957–1958), and H3N2 (1968–1969). Mammals, such as pigs, can serve as a “mixing vessel” between avian and human influenza viruses (Figure 1). Pigs can be infected with influenza viruses from both birds and people. If a pig is infected with both viruses at the same time, the two different viruses can recombine and give rise to new combinations that mix genetic materials and capabilities from the two parental viruses.

The Asian H5N1 strain has created new flu-transmission scenarios. The virus is able to directly infect people who have contact with infected poultry. As of July 2005, H5N1 has caused at least 109 human cases, over half of them fatal, in five Asian countries. The current H5N1 is primarily an avian virus, it is inefficiently transmitted to people and there is no evidence of sustained person-to-person transmission. The H5 hemagglutinin has not been widely circulated in humans, so people do not have cross-protective immunity. The concern is that if the H5N1 virus mutates or recombines with other strains of influenza A viruses,

perhaps one that spreads from person-to-person efficiently, the H5N1 virus may acquire such abilities and evolve to become the next pandemic strain.

Currently, the implications of HPAI H5N1 for North American wildlife remain unclear. If migratory birds carry and shed the virus along flyways, the potential exists for the virus to spread into additional migratory species and for the subsequent spread of the H5N1 virus into other parts of the world including Europe, Australia, and North America. It is unclear whether infected birds are capable of migration, and carrying and shedding the virus.

Bird migration is only one of the possible routes of introducing HPAI H5N1 to the North American continent. Travel by infected people, along with contaminated luggage or clothing, and transportation of infected poultry, including the smuggling of illegal pet birds, and other poultry equipment and products, are more direct means to transport the virus.

The USGS National Wildlife Health Center (NWHC) has the capability to detect HPAI H5N1 and is screening select submissions for avian influenza. The availability of molecular technology has enabled NWHC to test for the influenza viruses that carry the H5, H7 (another possible poultry pathogen) and N1 subtypes. The NWHC, with assistance from others, has begun to conduct targeted surveillance of aquatic birds for avian influenza and will continue to assist in disease investigations of wildlife mortality events. Also planned are experimental studies in wild waterfowl and other waterbirds to better understand the potential role of, and impact to, various North American waterbird species.



Chickens infected with H5N1. Note flaccid combs and the depressed and lethargic appearance of the lower chicken.

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